# Measuring physical activity and cardiovascular health in population-based cohort studies

CLS working paper number 2021/3

By Aaron Kandola & David Bann

CENTRE FOR LONGITUDINAL STUDIES

Economic and Social Research Council

**Corresponding author**

David Bann

UCL Centre for Longitudinal Studies

david.bann@ucl.ac.uk

This paper was written in June 2019, and published as a working paper in March 2021 by the UCL Centre for Longitudinal Studies.

UCL Social Research Institute

University College London

20 Bedford Way

London WC1H 0AL

www.cls.ucl.ac.uk

The UCL Centre for Longitudinal Studies (CLS) is an Economic and Social Research Council (ESRC) Resource Centre based at the UCL Social Research Institute, University College London. It manages four internationally-renowned cohort studies: the 1958 National Child Development Study, the 1970 British Cohort Study, Next Steps, and the Millennium Cohort Study. For more information, visit www.cls.ucl.ac.uk.

This document is available in alternative formats. Please contact the Centre for Longitudinal Studies.

Tel: +44 (0)20 7612 6875

Email: clsfeedback@ucl.ac.uk

## Disclaimer

This working paper has not been subject to peer review.

CLS working papers often represent preliminary work and are circulated to encourage discussion. Citation of such a paper should account for its provisional character. A revised version may be available directly from the author.

Any opinions expressed here are those of the author(s) and not those of the UCL Centre for Longitudinal Studies (CLS), the UCL Social Research Institute, University College London, or the Economic and Social Research Council.

## How to cite this paper

Kandola, A., Bann, D. (2021) *Measuring physical activity and cardiovascular health in population-based cohort studies.* CLS Working Paper 2021/3. London: UCL Centre for Longitudinal Studies.

# Contents

# 1. Physical activity

## 1.1. Introduction

Implicating physical activity in biomedical and health research relies upon accurate measurement. Efforts to develop better ways of measuring physical activity have come on the back of a widespread rise in sedentary lifestyles (Tremblay et al., 2011; Wilmot et al., 2012). The importance of physical activity is well-established in physical health (Arem et al., 2015) and is increasingly becoming recognised in mental health (Schuch et al., 2018).

Physical activity refers to any bodily movement produced by the skeletal muscles that requires energy expenditure (Caspersen, 1985). It is a complex construct that can be variably categorised qualitatively (e.g. incidental activity, or exercise), quantitatively (e.g. frequency, duration, or intensity), or contextually (e.g. time, place, position, or posture) (Butte et al., 2012).

Ultimately, a tool for assessing physical activity should be versatile, easy to interpret, and accurate in estimating intensity, volume, duration, and frequency of activity (Ainsworth et al., 2015). We conducted a non-systematic rapid review of the literature in this area to identify existing and novel methods of measuring physical activity in large-scale studies. The following sections will outline some commonly used methods for measuring physical activity in population-based cohort studies (e.g. accelerometers), along with some more novel approaches (e.g. combined monitors).

## 1.2. Findings

### 1.2.1. Gold standard

Gold standard measures of physical activity involve direct measures of energy expenditure through measures of metabolic processes. Calorimetry uses body heat in a sealed calorimetry chamber, whereas indirect calorimetry uses measures of oxygen and carbon dioxide in a respiration chamber. It is also possible to use doubly labelled water, where participants consume modified drinking water and collect daily urine samples that are analysed to derive carbon dioxide expiration. However, these are expensive and difficult to administer in the field at scale (Aparicio-Ugarriza et al., 2015).

### 1.2.2. Self-report measures

Self-report questionnaires have been most common method of collecting physical activity data in population-based research. The most widely used questionnaire is the International Physical Activity Questionnaire (IPAQ) (van Poppel et al., 2010). It contains 31 questions (9 in the short-form version) on time spent sitting, in light activity (e.g. walking), moderate activity (e.g. leisure cycling), and vigorous activity (e.g. running) over the past week or in a typical week. As self-report methods are subject to attentional biases (Prince et al., 2008) validation studies have found poor correlations with objective measures of activity, such as accelerometers (e.g. $r$ = 0.09 to 0.39) (Lee et al., 2011a).

However, self-report questionnaires have a low participant burden and can provide detail on the environmental and psychosocial context, and perceived intensity of physical activity. It is also possible to group patterns of activity together that may involve rapid fluctuations in intensity, or bouts of inactivity, such as gardening. Most physical activity guidelines are also based on data from self-report questionnaires, so they can be more comparable in studies using this type of data (Troiano et al., 2014).

### 1.2.3. Accelerometers

Accelerometers are electromechanical devices that measure bodily movements through changes in acceleration on one, or multiple planes, over time. They have become the preferred method of objectively estimating physical activity in field research (Hills et al., 2014). The monitor is worn on a part of the body most likely to capture movement (close to the its centre of gravity), usually the wrist or hip. It records any bodily acceleration as a 'count'. These counts are usually recorded in pre-specified time periods ('epochs'), usually of 1 minute, with counts per epoch taken to indicate magnitude of movement.

Validation studies have found that accelerometers have a moderate-to-strong correlation ($r$ = 0.45-0.93) with direct measures of oxygen consumption (e.g. doubly labelled water and indirect calorimetry) when estimating physical activity in children and adults (Trost et al., 2005).This variety is due to methodological differences such as the use of different devices, pre-processing and analysis, length of use, epoch definition, bodily placement (e.g. hip, or wrist), or the type of activities being monitored. Accelerometers have been used in several national cohort studies, such as in Canada (Collet et al., 2011) and the UK (O'Donovan et al., 2013).

Over 50% of published studies use ActiGraph accelerometers for measuring energy expenditure (Wijndaele et al., 2015). The latest models (GT3X, GT3X+, and wGT3X-BT) contain a triaxial sensor, meaning they can record acceleration over three planes. These are generally more accurate for estimating physical activity than earlier uniaxial models that only recorded acceleration on the vertical axis (Butte et al., 2012). Triaxial devices may also be more useful in children as it can capture jumping, and climbing behaviour (Hills et al., 2014). Compared with direct measures of oxygen consumption using gas analysis, the ActiGraph GT3X+ has a strong correlation ($r$ = 0.73) when estimating physical activity in a sample of 52 participants performing structures tasks (Bai et al., 2016). But the model performs poorly when estimating physical activity during higher intensity activities and field sports (Gastin et al., 2018).

Other types of accelerometer focus on approximating posture, which is more useful in studies of sedentary behaviour (Granat, 2012). The Intelligence Device for Energy Expenditure and physical Activity (IDEEA) uses multiple sensors located around the body, whereas other devices only use a single sensor, such as activPAL (Granat, 2012). ActivPAL is validated against direct observation using an automated camera for measure for measuring sedentary behaviour in 11 free living participants with 4.11% error (Kim et al., 2015).

Accelerometers are well established in research due to their ability to non-invasively collect reliable and detailed information on the frequency, duration, pattern and intensity of activity (Ainsworth et al., 2015). They can also estimate gait speed using cadence (steps/minute). Accelerometers may be the most practical way of measuring physical activity outside of a laboratory but are expensive compared to pedometers or self-report questionnaires.

In recent years, a range of commercial activity trackers containing accelerometers have become available that are inexpensive and have comparable accuracy to research-grade accelerometers (Evenson et al., 2015). Commercial monitors also have several other advantages, including real-time feedback, high ecological validity and excellent connectivity for syncing with mobile phones or computers. Their use in research is growing rapidly. In 2016, around 127 trials were registered using Fitbit activity monitors for a range of purposes, with the majority being physical activity monitoring for health purposes (Wright et al., 2017). There are a great range of different activity trackers, but vast majority of activity trackers are made by Fitbit or Jawbone who make up around 87% of the market share (Dolan, 2014).

A systematic review found that models from both brands are reliable step monitors (Pearson or interclass correlation coefficient >= 0.80) when validated against step counting or accelerometer steps, but error increases markedly at slower walking paces (Evenson et al., 2015). Two systematic reviews have found activity monitors tend to underestimate energy expenditure with Fitbit monitors being the most accurate (Bunn et al., 2018; Evenson et al., 2015). For estimating physical activity several Fitbit and Jawbone brands are validated against indirect calorimetry with studies including 52 (Bai et al., 2016) and 60 (Lee et al., 2014) participants finding 10-20% error in semi structured environments. Against doubly labelled water in 19 free living participants activity monitors underestimated physical activity by 590 to 69 kcal/day (Murakami et al., 2016). Compared with direct gas analysis the activity monitors underestimated physical activity by 13-29% in 30 participants in semi-structured environments (Imboden et al., 2018). This study also found they underestimated steps by 23 to 32% compared with direct observation. In general, commercial and research grade accelerometers perform at roughly the same level for estimating steps and energy expenditure.

However, broader problems with all accelerometers include the high variability in methods for processing and analysing the data (Troiano et al., 2014). This is further complicated by the use of different proprietary algorithms, such as for converting raw data to counts. For commercial grade accelerometers, the algorithms for determining steps and energy expenditure are typically not shared with researchers (Wright et al., 2017). There is no consensus on how commercial activity monitors calculate METs, which makes comparisons with other studies challenging.

Accelerometers are reliable measures of steps and can accurately distinguish between related activities such as walking and running. But most accelerometers only focus on lower-body movement (Aparicio-Ugarriza et al., 2015). They are poor at estimating non-ambulatory activities that may account for a substantial part of an individual's daily activity, such as cycling and resistance training. They are also less sensitive to sedentary, or light intensity activity, but some models have sought to address this limitation, such as ActivPal.

Compliance can also be problematic. A systematic review of two pedometer and eight accelerometer studies between 2012 and 2017 found a mean adherence of 59% (39.6% to 85.7%), but samples were predominantly males aged between 42 and 82 (Marin et al., 2019). But data from the US NHANES studies suggests that compliance rates are greater for wrist-worn accelerometers where 70-80% of participants provided sufficient data for analysis, compared to 40-70% with the hip-worn accelerometers (Troiano et al., 2014).

### 1.2.4. Pedometers

Traditional pedometers are small devices that detect vertical acceleration (movement up and down) from the hips. Each up and down movement is measured as a step count. They are particularly suited to measuring 'ambulatory' activities, such as walking or running (Tudor-Locke et al., 2002). More modern pedometers use a microelectromechanical system, and specialised algorithms that have greatly improved their accuracy (Ainsworth et al., 2015).

Compared against a manually counted steps on a treadmill, a study of 10 pedometers in 10 people found that they can accurately record steps (~1% error) and distance (~10% error), but performed worse at slower paces (Crouter et al., 2003). Two of the most commonly used pedometers are the Omron HJ and YAMAX DigiWalker range. These are validated against manual step counting on a treadmill with the Omron pedometer showing high consistency across all speeds (ICC = 0.90 – 0.99), and the YAMAX pedometer showing good consistency at higher speeds (ICC = 0.72 – 0.99) but less consistency at paces of less than 4km/h (ICC = 0.28- 0.53) (Lee et al., 2015). The poorer performance at slower paces means that pedometers may not be suitable for older populations, or those with abnormal gait speeds (Hills et al., 2014). Many population-based studies across the world have used pedometers on a large scale, such as in Australia (Dwyer et al., 2007) and the US (Bassett et al., 2010).

A great range of commercial pedometers are also now available, with some showing good validity. For example, the Fitbit Zip correlates well with a YAMAX pedometer and ActiGraph GR3X accelerometer for measuring steps at various speeds in free living conditions ($r$ = 0.91) (Tully et al., 2014).

Pedometers have some advantages over accelerometers. The most pertinent of which is price. This can be as low as £10 per unit, whereas accelerometers often cost over £100 per unit. Pedometers have traditionally been a more reliable measure of steps (Butte et al., 2012). One study comparing an accelerometer (ActiGraph GT3X) with a pedometer (DigiWalker SW-200) in overweight and obese adults found the pedometer to be more accurate when the total step volume was high or low, but the difference was small (Barreira et al., 2013).

However, pedometers are more limited than accelerometers as most models only detect acceleration across the vertical plane, i.e. detecting up and down movement. They are unable to fully capture physical activity due to their exclusive focus on steps (Ainsworth et al., 2015). Pedometers are also unable to provide supplementary detail on ambulatory activities, such as walking speed or stride length (Butte et al., 2012). This makes it difficult to estimate total distance travelled without prior calibration, which can be time-consuming.

The accuracy of modern accelerometers for measuring steps is becoming indistinguishable from pedometers (O'Neill et al., 2017), and they also provide other data that can be extrapolated to provide more meaningful information that steps. For example, they collect temporal information that allow for estimations of time spend in different activities. Modern triaxial accelerometers can also capture a much wider range of activity than steps as they record acceleration across three planes.

But this simplicity does mean that the data from pedometers is more comparable, straightforward to analyse, and has an easily interpretable unit of output (steps), than accelerometers (Ainsworth et al., 2015).

### 1.2.5. Heartrate monitors

Heart rate monitors are small, non-invasive devices that record heart rate. Unlike accelerometers and pedometers, they do not measure activity through detecting motion.

Minute-by-minute heart rate monitoring is another method for assessing physical activity. This assumes a linear relationship between heart rate and oxygen consumption (energy expenditure). Some studies have demonstrated this assumption to be valid across a range of activities (Livingston, 1997), with small variations due to factors such as age, fitness levels, and movement efficiency. Insufficient calibration can exaggerate these variations and caution is necessary when dealing with certain population groups, such as older populations (Schrack et al., 2014).

Calibration studies typically involve the simultaneous recording of heart rate, and oxygen consumption while performing various tasks at different intensities. Researchers typically use FLEX-HR to account for the overlap between active and sedentary heart rate. This assigns individually determined thresholds based on maximum resting heart rate, and minimum active heart rate. FLEX-HR has been validated against doubly labelled water with a similar predictive value for physical activity in eight young athletes (Ekelund et al., 2002). A range of commercial grade monitors also track heartrate with good accuracy. A recent systematic review indicates that commercial grade activity monitors are validated against ECG monitors (CC = 0.78 to 0.99) with the Polar H7 (CC = 0.99) and Apple Watch (CC = 0.92 to 0.98) being the most accurate brands (Bunn et al., 2018).

A key advantage of heart rate monitors is the ability to calibrate them to individuals, which can account for variation due to factors such as fitness (Hills et al., 2014). But this calibration procedure can be costly, and time-consuming. It is also possible to obtain good measures of exercise intensity, and both ambulatory and non-ambulatory activity types. But heart rate monitors are poor at estimating low intensity activity and can be disrupted by other factors than activity that affect heart rate, such as prescription drugs (Butte et al., 2012).

### 1.2.6. Combined monitors

Innovations for improving the collection of physical activity data is unlikely to occur from developing fundamentally new methods, but instead from modifying existing methods (Intille et al., 2012). Accelerometers, pedometers and heart rate monitors each have downsides that can be overcome through combining them with each other, or other devices. Multi-sensor systems involve the combination of multiple physiological and mechanical sensors, such as accelerometers, global positioning systems (GPS), heart rate, body temperature, and skin response monitors.

The most promising method is to combine heartrate monitors with accelerometers to improve accuracy. For example, using accelerometer data makes it possible to verify changes in heartrate are due to physical activity. Data from the heartrate monitor can help an accelerometer to capture non-ambulatory activities, such as cycling, or weightlifting. It can reduce measurement error across the whole spectrum of physical activity intensities as heartrate monitors are superior for measuring higher intensity activity, while accelerometers are superior for lower intensity activity (Ainsworth et al., 2015).

ActiHeart is the most widely used example of such a device. Compare with direct calorimetry, the ActiHeart device predicting energy expenditure with a very low error of 0.9% (SD = 10.3) in 109 children and adolescents (Zakeri et al., 2008). The error was not correlated with age or body mass, indicating a lack of systematic error. It is also validated against indirect calorimetry in 39 children showing a strong correlation with physical activity (R2 = 0.86), but this was a small improvement on models of activity alone without heartrate (R2 = 0.82) (Corder et al., 2005). Combining accelerometer and heartrate monitors consistently improve accuracy of physical activity than either method alone (Brage et al., 2005; Butte et al., 2012; Corder et al., 2005; Villars et al., 2012). The ActiHeart has been used in population-based cohorts before such as the National Survey of Health and Development in the UK with 1,727 participants (Cooper et al., 2015).

The device is validated against indirect calorimetry in adults (Casiraghi et al., 2013; Santos-Lozano et al., 2017), doubly labelled water in children (Calabro et al., 2013) and overweight and obese women (Slinde et al., 2013), sample sizes varied from 26 to 62. The measurement error varied from 10.9% to 20.7% depending on the model used and the device shows consistent individual variation when estimating energy expenditure. Similarly to accelerometers, the SenseWear Armband may not provide reliable estimates for physical activity during higher intensity activities and field sports (Gastin et al., 2018).

Multi-sensor systems improve accuracy, especially for non-ambulatory activities (Ainsworth et al., 2015) But they are more expensive and can increase participant burden if they involve the use of multiple devices, or more invasive devices. The development of commercial grade devices that combine accelerometers with heartrate monitors could be a useful option for reducing cost, but little work has been done to validate these devices so far. One study tested a range of commercial devices with heartrate monitors against a clinical pulse oximeter in four participants and found error ranged between 8.9 to 20.2% (El-Amrawy & Nounou, 2015). Another study with 24 participants compared the Fitbit and Basic Peak commercial devices to ECG and found strong correlations for both (r = 0.83 and 0.92, respectively) (Jo et al., 2016).

### 1.2.7. Mobile phones

There are also novel opportunities for data collection from the widespread use of mobile phones with a range of built-in sensors, good storage and battery capacities, built-in internet connectivity, location services, and fast processors (Intille et al., 2012). As many people already own a mobile phone, they are cost-effective and have a low participant burden. Their storage and connectivity capacities mean they are well suited to collecting and sending large amounts of data. The use of activity monitors can also cause participants to change their behaviour (Trost et al., 2005), but the use of mobile phones as a more passive measure may reduce this effect.

Several attempts to validate the use of mobile phones in tracking activity have been made. One study found the raw counts of android phones and an accelerometer (ActiGraph GT3X+) correlate strongly ($p$ = 0.77-0.82) in a laboratory and correlated moderately (p = 0.59-0.67) in free-living (Hekler et al., 2015). Other studies have found mean step count of iOS applications (Fitbit, Health Mate, Runtastic and Moves) and one Android application (Moves) varied between -6.7% and 6.2% compared with direct observation (Case et al., 2015), mean error when attached to the arm in one study was 0.7% (Presset et al., 2018). Other studies have found iPhone pedometers to be inaccurate compared to direct observation for measuring steps (Bergman et al., 2012; Balmain et al., 2019) and sensitivity ranging from 69.3% to 101.3% compared with pedometers (Boyce et al., 2012). There is also a large variety in the accuracy of different apps on the same device for measuring steps (Åkerberg et al., 2012; Leong & Wong, 2017).

A study in 2014 developed an algorithm to test the capacity of an iPhone/iPod to record activity type (walking or running), speed (kmh-1), and energy expenditure (METs) against indirect calorimetry (Nolan et al., 2014). They found high classification accuracy for identifying activity type (99%), a bias of 0.02kmh-1 (SE = 0.57 kmh-1) for speed, and bias of 0.35 METs (SE 0.75) for walking and -0.43 (SE 1.24) for running. The accuracy (between 91.7-100%) of iPhone/iPod for identifying common activity types, such as walking, jogging, and sitting has also been demonstrated elsewhere (Wu et al., 2012). A review of 10 studies found smartphone measurement accuracy for identifying activities ranges from 52 to 100% (Bort-Roig et al., 2014).

Many of these studies are on healthy young people. While these results may not be applicable to older populations or people with abnormal gait patterns (Brodie et al., 2018) mobile phones are highly customisable. There are opportunities for researchers to develop their own software using raw sensor data through platforms such as Apple's Research Kit and Care Kit (Wright et al., 2017). These platforms are tailored to biomedical and health research and have already shown great potential. For example, mPower app is designed to study sleep, exercise, mood and movement data in people with Parkinson's disease and already has over 10,000 users (Bot et al., 2016).

The scalability of physical activity monitoring is demonstrated by a recent study by Althoff *et al.* (2017) who collected mobile phone data using the Azumio app on the physical activity of 727,527 people from 46 countries. But at the time, Azumio was not validated. Brodie *et al.* (2018) found significant undercounting by Apple phones using the Azumio app, with median accuracy ranging from 15 to 66%. Median accuracy for Android phones was 38% to 100% compared with direct observation. There also seems to be great variety in the accuracy of different apps and different positions of the phone (Åkerberg et al., 2012; Leong & Wong, 2017).

## 1.3. Conclusions

Measuring physical activity in population-based cohorts has advanced greatly from the shift to objective measures. Accelerometers may currently be the best option for estimating physical activity in field research. Newer triaxial models provide greater accuracy and versatility than pedometers, but this comes with an increase in price. Pedometers are still a reliable option for providing a cost-effective measure of steps, which can be used to estimate physical activity. Commercial grade accelerometers are another option that could reduce cost without compromising reliability. Accuracy may be further increased through the use of more expensive combined monitors, such as ActiHeart. But it is unclear whether the modest increases in accuracy justify the price difference.

The use of mobile phones has an enormous potential for collecting physical activity data in large cohorts at minimal cost and low participant burden. However, the reliability of these methods is still a major concern.

# 2. Cardiovascular health

## 2.1. Introduction

Cardiovascular health refers to the functioning of the circulatory system, which comprises of the heart and blood vessels. The circulatory system transports oxygen and nutrients through the bloodstream to tissues around the body and removes carbon dioxide and other waste products.

Dysfunction in the cardiovascular system is severe and can be fatal. Cardiovascular disease (CVD) is the leading cause of mortality worldwide, which accounts for 17.9 million deaths each year, representing 31% of all deaths worldwide (WHO, 2018). CVD refers to a group of conditions that affect the heart and blood vessels.

A range of genetic, environmental and behavioural factors affect the risk of CVD. These can be modifiable risk factors such as physical inactivity, or non-modifiable factors such as age (WHO, 2017). The culmination of these known factors is directly observable through a collection of biological indicators that can be measured to determine a person’s cardiovascular risk profile. There are a great range of different models for predicting CVD, with the most recent systematic review finding 363 validated prediction models (Damen et al., 2016). Most models include age, smoking status, blood pressure and cholesterol levels. But this review identified over 100 additional factors that are only included in one or two models. This demonstrates both the complexity of quantifying CVD risk and the empirical focus on developing novel methods for understanding and predicting CVD.

Here, we conducted a non-systematic rapid review of the literature in this area to identify novel methods of measuring cardiovascular health in large-scale studies.

## 2.2. Findings

### 2.2.1. Lipids and lipoproteins

Fats such as cholesterol and triglycerides are essential to proper functioning and can be absorbed from foods or synthesized in the liver, or other parts of the body. They are transported through the bloodstream by lipoprotein particles, which can be Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), Intermediate-density lipoprotein (IDL), High Density Lipoprotein (HDL). The proportion of these particles in the blood is a well-established indicator of CVD and routinely measured in clinical settings. The proportion of HDL to total cholesterol in the blood is a strong, independent predictor of CVD and cardiovascular events (Barter et al., 2007; Pischon et al., 2005).

More recently, other lipids important to cardiovascular functioning have emerged as independent risk factors for CVD, such as Lipoprotein a (LP(a)) (Tsimikas & Hall, 2012). All non-HDL lipoproteins, including LP(a), contain a single apolipoprotein B (ApoB) molecule. This means it is possible to count exactly how many non-HDL transporters there are in the bloodstream. Evidence is accumulating that ApoB or the ratio of ApoB to ApoA1 is an even stronger predictor of CVD than traditional measures of HDL and total cholesterol (Contois et al., 2009; McQueen et al., 2008).

A better understanding of the factors that influence lipid profiles on a population-level will be crucial to the prevention of CVD.

### 2.2.2. Gold standard

The gold standard for collecting blood plasma or serum is through venepuncture. But this can be costly and has a high participant burden.

### 2.2.3. Options in the field

Dried blood spots (DBS) are a method of collecting drops of blood from a skin prick, usually administered to the finger or ankle with a sterile lancet. The blood spots are collected and dried on a piece of filter paper. The total cost of supplies is around $2 per participant, it is less invasive than venepuncture and the risk of blood-borne pathogens is reduced (McDade et al., 2013). The procedure is straightforward and can be collected by a trained interviewer, or in some cases by the participant themselves. DBS tests are a low-cost method of blood sampling in field settings that can be administered in large population-based studies (McDade et al., 2007). Depending on the biomarkers of interest, a research-grade freezer may be necessary to ensure minimal degradation of the sample. DBS have been used in large population-based surveys, such as the National Longitudinal Study of Adolescent Health and the Health and Retirement Study including data from 15,701 participants (Nguyen et al., 2014).

The biomarkers detectable through DBS are more limited, but advanced analytical methods are improving the accuracy and range of detectable biomarkers (Henderson et al., 2017). Compared with venepuncture, it is possible to achieve good accuracy in detecting levels of haemoglobin A1c (HbA1c) ($r$ = 0.85-0.92), C-reactive protein (CRP) ($r$ = 0.84), ApoA1 ($r$ = 0.86), ApoB ($r$ = 0.83) and glucose ($r$ = 0.81) in studies containing between 35 to 317 samples (Eick et al., 2017; Henderson et al., 2017; Lacher et al., 2013; Miller et al., 2015). CRP is a widely used inflammatory marker and HbA1c is a surrogate measure for glucose control over a three to four month period, used as a biomarker for diabetes diagnoses (Rahber, 2005). The accuracy is more varied for detecting total cholesterol ($r$ = 0.34-0.89) and HDL cholesterol ($r$ = 0.30-0.72).

There is considerable heterogeneity in the methods used for preparing and analysing DBS samples (Affan et al., 2014). Studies are starting to focus on validating DBS using accessible, cost-effective methods of analysis, such as enzyme-linked immunosorbent assay (ELISA) (Eick et al., 2017). But DBS analysis methods remain subject to significant individual or sample variability, despite good linear correlations with venepuncture (Henderson et al., 2017).

#### 2.2.4. Blood pressure

Blood pressure refers to the pressure generated by the heart to move blood around the circulatory system. High blood pressure places excess strain on circulatory system that can lead to damage tissue and the accumulation of plaques that narrow the arteries. High blood pressure, or hypertension, increases the risk of CVD (Kannel, 1996; Vasan et al., 2001) and is among the most important predictors of cardiovascular health (Damen et al., 2016; Wilson et al., 1998).

#### 2.2.5. Gold standard

The gold standard measure of blood pressure is mercury sphygmomanometers but concerns over the safety of mercury has led to the development of non-mercury sphygmomanometers and other methods (Arakawa et al., 2018). These methods all involve a sphygmomanometer with an inflatable cuff that is inflated around the arm to compress the artery and cut off the blood flow. As the cuff is slowly deflated, blood flow returns to the artery and different devices can be used to detect systolic and diastolic blood pressure.

While these methods are accurate, they require specialist equipment, must be performed by a medical worker and can be uncomfortable due to cuff inflation. They are only able to give a discreet measurement of blood pressure at one time. Most blood pressure readings are conducted in a medical environment, which may itself cause error due to discomfort or anxiety.

#### 2.2.6. Options in the field

Several devices for measuring blood pressure without a cuff have been developed to allow continuous monitoring outside of medical settings. These devices are typically measure the time it takes for a volume of blood to move from the heart to a peripheral organ, yielding metrics such as pulse transit time and pulse arrival time (Sharma et al., 2017). These times can be used to estimate blood pressure through arterial compliance,

One promising new multimodal wrist-based biosensor uses a combination of photoplethysmography and impedance plethysmography to estimate blood pressure (Rachim & Chung, 2019). In a validation study with 10 participants, the device performed well against an ambulatory blood pressure monitor for measuring systolic ($r$ = 0.81) and diastolic ($r$ = 0.78) blood pressure. Another promising device is the Freescan self-blood monitor (Maisense Inc., Taiwan). After initial calibration with basic anthropomorphic information, this handheld monitor uses three electrodes and a force sensor to estimate blood pressure when held to the radial pulse on the wrist. Compared with a mercury sphygmomanometer, the Freescan device estimated blood pressure well in ~80% of participants (n = 85), with mean difference of − 0.6 ± 1.6 mmHg for systolic and 0.5 ± 1.8 mmHg for diastolic blood pressure (Boubouchairopoulou et al., 2017). Another cuffless device is the Somnotouch-NIBP (Randersacker, Germany) which has been measured over a 24-hour period in a sample of 71 participants (Krisai et al., 2019). Against a validated cuff-based oscillometric device, there was a mean absolute difference between systolic blood pressure of 10.2 mmHg and 8.2 mmHG with diastolic blood pressure with Somnotouch-

NIBP. The difference was significant in clinical practice and further work is required to fully validate this device.

There are many cuffless devices being developed and accuracy is improving (Arakawa et al., 2018). But many are in a prototypical stage of development and few have been validated in clinical settings (Schoot et al., 2016). They are also costly, which may be prohibitive for population-based research at this stage.

### 2.2.7. Cardiorespiratory fitness

Cardiorespiratory fitness (CRF) is the capacity of the cardiovascular and respiratory systems to supply oxygen to muscles and other bodily tissues, typically during exertion (Blair et al., 1996). It is an objective measure of heart, lung and skeletal muscle efficiency. CRF is consistently associated with an elevated risk of CVD, cardiovascular events and all-cause mortality across all age groups in a series of prospective, longitudinal studies (Blair et al., 1996; Berry et al., 2013; Carnethon et al., 2003, 2005; Kodama et al., 2009; Lee et al., 2011; Mora et al., 2003). In one prospective study including 211,996 person-years of data, low CRF (RR, 1.52; 95% CI, 1.28-1.82) was a stronger predictor of CVD than smoking (RR, 1.65; 95% CI, 1.39-1.97), chronic illness (RR, 1.63; 95% CI, 1.37-1.95), increased cholesterol level (RR, 1.34; 95% CI, 1.13-1.59), and elevated systolic blood pressure (RR, 1.34; 95% CI, 1.13-1.59) (Blair et al., 1996). Another prospective study with 21,080 participants, the adding CRF to standard clinical risk factors significantly improved CVD classification by 37%, and low CRF was the strongest predictor of CVD (HR, 1.91; 95% CI 1.74-2.09) of all other variables in the model (Myers et al., 2017). This relationship is likely due to the broad influence that CRF has on an array of cardiovascular risk factors, including insulin sensitivity, blood lipid and lipoprotein profile, blood pressure, body composition and inflammation (DeFina et al., 2015; Lee et al., 2010; Myers et al., 2015).

The primary determinant of CRF is physical activity (Carrick-Ranson, et al., 2014) and the American Heart Association recently included physical activity as a clinical indicator of cardiovascular risk along with traditional risk factors, such as blood pressure (Strath et al., 2013). CRF can be used as a surrogate measure of habitual physical activity that objectively encapsulates trends over time. But CRF is more than a marker of habitual physical activity (DeFina et al., 2015; Myers et al., 2015). CRF has been found to be a stronger predictor of cardiovascular events than physical activity (Myers et al., 2017; Swift et al., 2013). In addition to physical activity trends, CRF also encapsulates interactions between a range of other factors important to cardiovascular health, such as smoking and adiposity (DeFina et al., 2015). There is also a large genetic component to CRF, that could account for as much as 49% of variation in CRF between individuals (Bouchard et al., 2011).

Many now believe that the importance of CRF has been overlooked and should be included as an independent clinical risk factor for CVD (Blair et al., 2009; DeFina et al., 2015; Lee et al., 2010; Myers et al., 2015). Part of the reason CRF has been overlooked is a lack of large population-based research due to the difficulty of administering gold standard CRF measures at scale.

### 2.2.8. Gold standard

Gold standard measures of CRF use a maximal exercise test protocol with gas analysis (American College of Sports Medicine, 2013). But these tests are expensive and difficult to administer in population-based cohorts.

### 2.2.9. Options in the field

It is possible to estimate CRF with minimal equipment through methods that determine oxygen consumption through measuring performance on field tests. Many of these tests involve walking or running certain distances or for certain time periods, the results of which are compared with direct measures of oxygen consumption. The 20m shuttle run test is one of the most common examples (Castro-Pinero et al., 2010). The test involves one-minute stages of continuous running between two lines 20 meters apart. The pace is set using audio cues, starting at 8.5km/h and increasing 0.5km/h every minute (Leger et al., 1984). It is possible to use this test in large groups simultaneously, with minimal equipment or training. A meta-analysis including 57 studies found that compared to direct, laboratory-based measures the 20m shuttle run test to have a moderate to high validity for estimating oxygen uptake ($r$ = 0.66-0.84), which increased when considering sex age and body mass ($r$ = 0.78-0.95) and was significantly more accurate in adults ($r$ = 0.94, CI 0.87-1.00) than for children ($r$ = 0.78, CI 0.72-0.85) (Mayorga-Vega et al., 2015). Submaximal step tests are another method of estimating CRF, where participants step up and down on a platform. One systematic review found these tests to have a moderate to strong correlation with direct measures of maximal oxygen uptake, depending on the protocol ($r$ = 0.47-0.95) (Bennett et al., 2016).

Another meta-analysis including 122 studies comparing walk/run tests against direct measures of oxygen consumption found the 1.5 mile and 12-minute walk/run test were significantly more accurate than all other forms of the test (Mayorga-Vega et al., 2016). These test variants involve either walking or running for 1.5-miles or 12 minutes, with time to completion or distance travelled taken to estimate CRF. According to the meta-analysis, both the 1.5-mile test ($r$ = 0.79, CI 0.73-0.85) and the 12-minute test ($r$ = 0.78, CI 0.72-0.83) have a moderate to high validity estimating oxygen uptake, based on 18 and 26 studies respectively.

## 2.3. Conclusions

Cardiovascular health is challenging to measure in populations due to the great variety contributing factors. Dried blood spots are a promising method of collecting blood lipids on a large scale, with comparatively low costs. It is even possible for samples to be collected by participants themselves. Advances in analytical techniques have greatly increase the number of relevant biomarkers that can be obtained through dried blood spots, maintaining good comparability with gold standard measures. Blood pressure is another important marker of cardiovascular health. While cuffless devices could be a useful method in the future, their reliability, cost, and practicality in large-scale studies is still unclear. CRF has long been overlooked as a predictor of CVD, possibly due to the impracticalities of administering gold standard exercise tests. But the 20m shuttle run, 1.5 mile walk/run and 12-minute walk/run are promising methods for estimating oxygen consumption on a large scale at low cost.

# 3. References


Affan, E. T., Praveen, D., Chow, C. K., & Neal, B. C. (2014). Comparability of HbA1c and lipids measured with dried blood spot versus venous samples: a systematic review and meta-analysis. *BMC Clinical Pathology*, *14*(1), 21. https://doi.org/10.1186/1472-6890-14-21

Ainsworth, B., Cahalin, L., Buman, M., & Ross, R. (2015). The Current State of Physical Activity Assessment Tools. *Progress in Cardiovascular Diseases*, *57*(4), 387–395. https://doi.org/10.1016/J.PCAD.2014.10.005

Åkerberg, A., Lindén, M., & Folke, M. (2012). How Accurate are Pedometer Cell Phone Applications? *Procedia Technology*, *5*, 787–792. https://doi.org/10.1016/J.PROTCY.2012.09.087

Althoff, T., Sosič, R., Hicks, J. L., King, A. C., Delp, S. L., & Leskovec, J. (2017). Large-scale physical activity data reveal worldwide activity inequality. *Nature*, *547*(7663), 336–339. https://doi.org/10.1038/nature23018

Aparicio-Ugarriza, R., Mielgo-Ayuso, J., Benito, P. J., Pedrero-Chamizo, R., Ara, I., González-Gross, M., & EXERNET Study Group. (2015). Physical activity assessment in the general population; instrumental methods and new technologies. *Nutricion Hospitalaria*, *31 Suppl 3*, 219–226. https://doi.org/10.3305/nh.2015.31.sup3.8769

Arakawa, T., Arakawa, & Toshiya. (2018). Recent Research and Developing Trends of Wearable Sensors for Detecting Blood Pressure. *Sensors*, *18*(9), 2772. https://doi.org/10.3390/s18092772

Arem, H., Moore, S. C., Patel, A., Hartge, P., Berrington de Gonzalez, A., Visvanathan, K., … Matthews, C. E. (2015). Leisure Time Physical Activity and Mortality. *JAMA Internal Medicine*, *175*(6), 959. https://doi.org/10.1001/jamainternmed.2015.0533

Bai, Y., Welk, G. J., Nam, Y. H., Lee, J. A., Lee, J.-M., Kim, Y., … Dixon, P. M. (2016). Comparison of Consumer and Research Monitors under Semistructured Settings. *Medicine & Science in Sports & Exercise*, *48*(1), 151–158. https://doi.org/10.1249/MSS.0000000000000727

Balmain, B., Tuttle, N., Bailey, J., Cheng, K., Duryea, M., Houlihan, J., … Morris, N. (2019). Using Smart Socks to Detect Step-count at Slow Walking Speeds in Healthy Adults. *International Journal of Sports Medicine*, *40*(02), 133–138. https://doi.org/10.1055/a-0732-5621

Barreira, T. V., Tudor-Locke, C., Champagne, C. M., Broyles, S. T., Johnson, W. D., & Katzmarzyk, P. T. (2013). Comparison of GT3X Accelerometer and YAMAX Pedometer Steps/Day in a Free-Living Sample of Overweight and Obese Adults. *Journal of Physical Activity and Health*, *10*(2), 263–270. https://doi.org/10.1123/jpah.10.2.263

Barter, P., Gotto, A. M., LaRosa, J. C., Maroni, J., Szarek, M., Grundy, S. M., … Fruchart, J.-C. (2007). HDL Cholesterol, Very Low Levels of LDL Cholesterol, and Cardiovascular Events. *New England Journal of Medicine*, *357*(13), 1301–1310. https://doi.org/10.1056/NEJMoa064278

Bassett, D. R., Wyatt, H. R., Thompson, H., Peters, J. C., Hill, J. O., & Hill, J. O. (2010). Pedometer-measured physical activity and health behaviors in U.S. adults. *Medicine and Science in Sports and Exercise*, *42*(10), 1819–1825. https://doi.org/10.1249/MSS.0b013e3181dc2e54

Bennett, H., Parfitt, G., Davison, K., & Eston, R. (2016). Validity of submaximal step tests to estimate maximal oxygen uptake in healthy adults. *Sports Medicine*, *46*(5), 737-750.

Bergman, R. J., Spellman, J. W., Hall, M. E., & Bergman, S. M. (2012). Is There a Valid App for That? Validity of a Free Pedometer iPhone Application. *Journal of Physical Activity and Health*, *9*(5), 670–676. https://doi.org/10.1123/jpah.9.5.670

Berry, J. D., Pandey, A., Gao, A., Leonard, D., Farzaneh-Far, R., Ayers, C., … Willis, B. (2013). Physical Fitness and Risk for Heart Failure and Coronary Artery Disease. *Circulation: Heart Failure*, *6*(4), 627–634. https://doi.org/10.1161/CIRCHEARTFAILURE.112.000054

Blair, S. N. (2009). Physical inactivity: the biggest public health problem of the 21st century. *British Journal of Sports Medicine*, *43*(1), 1–2. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19136507

Blair, S. N., Kampert, J. B., Kohl, H. W., Barlow, C. E., Macera, C. A., Paffenbarger, R. S., & Gibbons, L. W. (1996). Influences of Cardiorespiratory Fitness and Other Precursors on Cardiovascular Disease and All-Cause Mortality in Men and Women. *JAMA: The Journal of the American Medical Association*, *276*(3), 205. https://doi.org/10.1001/jama.1996.03540030039029

Bort-Roig, J., Gilson, N. D., Puig-Ribera, A., Contreras, R. S., & Trost, S. G. (2014). Measuring and Influencing Physical Activity with Smartphone Technology: A Systematic Review. *Sports Medicine*, *44*(5), 671–686. https://doi.org/10.1007/s40279-014-0142-5

Bot, B. M., Suver, C., Neto, E. C., Kellen, M., Klein, A., Bare, C., … Trister, A. D. (2016). The mPower study, Parkinson disease mobile data collected using ResearchKit. *Scientific Data*, *3*(1), 160011. https://doi.org/10.1038/sdata.2016.11

Boubouchairopoulou, N., Kollias, A., Chiu, B., Chen, B., Lagou, S., Anestis, P., & Stergiou, G. S. (2017). A novel cuffless device for self-measurement of blood pressure: concept, performance and clinical validation. *Journal of Human Hypertension*, *31*(7), 479–482. https://doi.org/10.1038/jhh.2016.101

Bouchard, C., Sarzynski, M. A., Rice, T. K., Kraus, W. E., Church, T. S., Sung, Y. J., … Rankinen, T. (2011). Genomic predictors of the maximal $O_2$ uptake response to standardized exercise training programs. *Journal of Applied Physiology*, *110*(5), 1160–1170. https://doi.org/10.1152/japplphysiol.00973.2010

Boyce, G., Padmasekara, G., & Blum, M. (2012). Accuracy of Mobile Phone Pedometer Technology. *Journal of Mobile Technology in Medicine*, 16–22. https://doi.org/10.7309/jmtm.13

Brage, S., Brage, N., Franks, P. W., Ekelund, U., & Wareham, N. J. (2005). Reliability and validity of the combined heart rate and movement sensor Actiheart. *European Journal of Clinical Nutrition*, *59*(4), 561–570. https://doi.org/10.1038/sj.ejcn.1602118

Brodie, M. A., Pliner, E. M., Ho, A., Li, K., Chen, Z., Gandevia, S. C., & Lord, S. R. (2018). Big data vs accurate data in health research: Large-scale physical activity monitoring, smartphones, wearable devices and risk of unconscious bias. *Medical Hypotheses*, *119*, 32–36. https://doi.org/10.1016/J.MEHY.2018.07.015

Bunn, J. A., Navalta, J. W., Fountaine, C. J., & Reece, J. D. (2018). Current State of Commercial Wearable Technology in Physical Activity Monitoring 2015-2017. *International Journal of Exercise Science*, *11*(7), 503–515. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/29541338

Butte, N. F., Ekelund, U., & Westerterp, K. R. (2012). Assessing physical activity using wearable monitors: measures of physical activity. *Medicine and Science in Sports and Exercise*, *44*(1 Suppl 1), S5-12. https://doi.org/10.1249/MSS.0b013e3182399c0e

Calabró, M. A., Stewart, J. M., & Welk, G. J. (2013). Validation of Pattern-Recognition Monitors in Children Using Doubly Labeled Water. *Medicine & Science in Sports & Exercise*, *45*(7), 1313–1322. https://doi.org/10.1249/MSS.0b013e31828579c3

Carnethon, M. R., Gidding, S. S., Nehgme, R., Sidney, S., David R. Jacobs, J., & Liu, K. (2003). Cardiorespiratory Fitness in Young Adulthood and the Development of Cardiovascular Disease Risk Factors. *JAMA*, *290*(23), 3092. https://doi.org/10.1001/jama.290.23.3092

Carnethon, M. R., Gulati, M., & Greenland, P. (2005). Prevalence and Cardiovascular Disease Correlates of Low Cardiorespiratory Fitness in Adolescents and Adults. *JAMA*, *294*(23), 2981. https://doi.org/10.1001/jama.294.23.2981

Carrick-Ranson, G., Hastings, J. L., Bhella, P. S., Fujimoto, N., Shibata, S., Palmer, M. D., … Levine, B. D. (2014). The effect of lifelong exercise dose on cardiovascular function during exercise. *Journal of Applied Physiology*, *116*(7), 736–745. https://doi.org/10.1152/japplphysiol.00342.2013

Case, M. A., Burwick, H. A., Volpp, K. G., & Patel, M. S. (2015). Accuracy of Smartphone Applications and Wearable Devices for Tracking Physical Activity Data. *JAMA*, *313*(6), 625. https://doi.org/10.1001/jama.2014.17841

Casiraghi, F., Lertwattanarak, R., Luzi, L., Chavez, A. O., Davalli, A. M., Naegelin, T., … Folli, F. (2013). Energy expenditure evaluation in humans and non-human primates by SenseWear Armband. Validation of energy expenditure evaluation by SenseWear Armband by direct comparison with indirect calorimetry. *PloS One*, *8*(9), e73651. https://doi.org/10.1371/journal.pone.0073651

Caspersen, C. J., Powell, K. E., & Christenson, G. M. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public health reports*, *100*(2), 126.

Castro-Piñero, J., Artero, E. G., España-Romero, V., Ortega, F. B., Sjöström, M., Suni, J., & Ruiz, J. R. (2010). Criterion-related validity of field-based fitness tests in youth: a systematic review. *British Journal of Sports Medicine*, *44*(13), 934–943. https://doi.org/10.1136/bjsm.2009.058321

Colley, R. C., Garriguet, D., Janssen, I., Craig, C. L., Clarke, J., & Tremblay, M. S. (2011). Physical activity of Canadian adults: accelerometer results from the 2007 to 2009

Canadian Health Measures Survey. *Health Reports*, *22*(1), 7–14. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21510585

Contois, J. H., McConnell, J. P., Sethi, A. A., Csako, G., Devaraj, S., Hoefner, D. M., … AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. (2009). Apolipoprotein B and Cardiovascular Disease Risk: Position Statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. *Clinical Chemistry*, *55*(3), 407–419. https://doi.org/10.1373/clinchem.2008.118356

Cooper, A. J. M., Simmons, R. K., Kuh, D., Brage, S., Cooper, R., & team, N. scientific and data collection. (2015). Physical Activity, Sedentary Time and Physical Capability in Early Old Age: British Birth Cohort Study. *PLOS ONE*, *10*(5), e0126465. https://doi.org/10.1371/journal.pone.0126465

Corder, K., Brage, S., Wareham, N. J., & Ekelund, U. (2005). Comparison of physical activity from combined and separate heart rate and movement models in children. *Medicine and Science in Sports and Exercise*, *37*(10), 1761–1767. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16260978

Crouter, S. E., Schneider, P. L., Karabulut, M., & Bassett, D. R. (2003). Validity of 10 electronic pedometers for measuring steps, distance, and energy cost. *Medicine and Science in Sports and Exercise*, *35*(8), 1455–1460. https://doi.org/10.1249/01.MSS.0000078932.61440.A2

Damen, J. A. A. G., Hooft, L., Schuit, E., Debray, T. P. A., Collins, G. S., Tzoulaki, I., … Moons, K. G. M. (2016). Prediction models for cardiovascular disease risk in the general population: systematic review. *BMJ (Clinical Research Ed.)*, *353*, i2416. https://doi.org/10.1136/bmj.i2416

DeFina, L. F., Haskell, W. L., Willis, B. L., Barlow, C. E., Finley, C. E., Levine, B. D., & Cooper, K. H. (2015). Physical Activity Versus Cardiorespiratory Fitness: Two (Partly) Distinct Components of Cardiovascular Health? *Progress in Cardiovascular Diseases*, *57*(4), 324–329. https://doi.org/10.1016/J.PCAD.2014.09.008

Dolan, L. Fitbit, Jawbone, Nike had 97 percent of fitness tracker retail sales in 2013. http://mobihealthnews.com/28825/fitbit-jawbone-nike-had-97-percent-of-fitness-tracker-retail-sales-in-2013/ (January 15, 2014).

Dwyer, T., Hosmer, D., Hosmer, T., Venn, A. J., Blizzard, C. L., Granger, R. H., … Dunstan, D. (2007). The inverse relationship between number of steps per day and obesity in a population-based sample – the AusDiab study. *International Journal of Obesity*, *31*(5), 797–804. https://doi.org/10.1038/sj.ijo.0803472

Eick, G. N., Kowal, P., Barrett, T., Thiele, E. A., & Snodgrass, J. J. (2017). Enzyme-Linked Immunoassay-Based Quantitative Measurement of Apolipoprotein B (ApoB) in Dried Blood Spots, a Biomarker of Cardiovascular Disease Risk. *Biodemography and Social Biology*, *63*(2), 116–130. https://doi.org/10.1080/19485565.2017.1283582

Ekelund, U., Yngve, A., Westerterp, K., & Sjöström, M. (2002). Energy expenditure assessed by heart rate and doubly labeled water in young athletes. *Medicine and Science in Sports and Exercise*, *34*(8), 1360–1366. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12165693

El-Amrawy, F., & Nounou, M. I. (2015). Are Currently Available Wearable Devices for Activity Tracking and Heart Rate Monitoring Accurate, Precise, and Medically Beneficial? *Healthcare Informatics Research*, *21*(4), 315–320. https://doi.org/10.4258/hir.2015.21.4.315

Evenson, K. R., Goto, M. M., & Furberg, R. D. (2015). Systematic review of the validity and reliability of consumer-wearable activity trackers. *International Journal of Behavioral Nutrition and Physical Activity*, *12*(1), 159. https://doi.org/10.1186/s12966-015-0314-1

Gastin, P. B., Cayzer, C., Dwyer, D., & Robertson, S. (2018). Validity of the ActiGraph GT3X+ and BodyMedia SenseWear Armband to estimate energy expenditure during physical activity and sport. *Journal of Science and Medicine in Sport*, *21*(3), 291–295. https://doi.org/10.1016/J.JSAMS.2017.07.022

Granat, M. H. (2012). Event-based analysis of free-living behaviour. *Physiological Measurement*, *33*(11), 1785–1800. https://doi.org/10.1088/0967-3334/33/11/1785

Hekler, E. B., Buman, M. P., Grieco, L., Rosenberger, M., Winter, S. J., Haskell, W., & King, A. C. (2015). Validation of Physical Activity Tracking via Android Smartphones Compared to ActiGraph Accelerometer: Laboratory-Based and Free-Living Validation Studies. *JMIR MHealth and UHealth*, *3*(2). https://doi.org/10.2196/MHEALTH.3505

Henderson, C. M., Bollinger, J. G., Becker, J. O., Wallace, J. M., Laha, T. J., MacCoss, M. J., & Hoofnagle, A. N. (2017). Quantification by nano liquid chromatography parallel reaction monitoring mass spectrometry of human apolipoprotein A-I, apolipoprotein B, and hemoglobin A1c in dried blood spots. *PROTEOMICS - Clinical Applications*, *11*(7–8), 1600103. https://doi.org/10.1002/prca.201600103

Hills, A. P., Mokhtar, N., & Byrne, N. M. (2014). Assessment of physical activity and energy expenditure: an overview of objective measures. *Frontiers in Nutrition*, *1*, 5. https://doi.org/10.3389/fnut.2014.00005

Imboden, M. T., Nelson, M. B., Kaminsky, L. A., & Montoye, A. H. (2018). Comparison of four Fitbit and Jawbone activity monitors with a research-grade ActiGraph accelerometer for estimating physical activity and energy expenditure. *British Journal of Sports Medicine*, *52*(13), 844–850. https://doi.org/10.1136/bjsports-2016-096990

Intille, S. S., Lester, J., Sallis, J. F., & Duncan, G. (2012). New Horizons in Sensor Development. *Medicine & Science in Sports & Exercise*, *44*(1 Suppl 1), S24–S31. https://doi.org/10.1249/MSS.0b013e3182399c7d

Jo, E., Lewis, K., Directo, D., Kim, M. J., & Dolezal, B. A. (2016). Validation of Biofeedback Wearables for Photoplethysmographic Heart Rate Tracking. *Journal of Sports Science & Medicine*, *15*(3), 540–547. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/27803634

Kannel, W. B. (1996). Blood Pressure as a Cardiovascular Risk Factor. *JAMA*, *275*(20), 1571. https://doi.org/10.1001/jama.1996.03530440051036

Kim, Y., Barry, V. W., & Kang, M. (2015). Validation of the ActiGraph GT3X and activPAL Accelerometers for the Assessment of Sedentary Behavior. *Measurement in Physical Education and Exercise Science*, *19*(3), 125–137. https://doi.org/10.1080/1091367X.2015.1054390

Kodama, S., Saito, K., Tanaka, S., Maki, M., Yachi, Y., Asumi, M., … Sone, H. (2009). Cardiorespiratory Fitness as a Quantitative Predictor of All-Cause Mortality and Cardiovascular Events in Healthy Men and Women. *JAMA*, *301*(19), 2024. https://doi.org/10.1001/jama.2009.681

Krisai, P., Vischer, A. S., Kilian, L., Meienberg, A., Mayr, M., & Burkard, T. (2019). Accuracy of 24-hour ambulatory blood pressure monitoring by a novel cuffless device in clinical practice. *Heart*, *105*(5), 399–405. https://doi.org/10.1136/HEARTJNL-2018-313592

Lacher, D. A., Berman, L. E., Chen, T.-C., & Porter, K. S. (2013). Comparison of dried blood spot to venous methods for hemoglobin A1c, glucose, total cholesterol, high-density lipoprotein cholesterol, and C-reactive protein. *Clinica Chimica Acta*, *422*, 54–58. https://doi.org/10.1016/J.CCA.2013.03.032

Lee, D., Artero, E. G., Xuemei Sui, X., & Blair, S. N. (2010). Review: Mortality trends in the general population: the importance of cardiorespiratory fitness. *Journal of Psychopharmacology*, *24*(4_suppl), 27–35. https://doi.org/10.1177/1359786810382057

Lee, D., Sui, X., Artero, E. G., Lee, I.-M., Church, T. S., McAuley, P. A., … Blair, S. N. (2011b). Long-Term Effects of Changes in Cardiorespiratory Fitness and Body Mass Index on All-Cause and Cardiovascular Disease Mortality in Men. *Circulation*, *124*(23), 2483–2490. https://doi.org/10.1161/CIRCULATIONAHA.111.038422

Lee, J. A., Williams, S. M., Brown, D. D., & Laurson, K. R. (2015). Concurrent validation of the Actigraph gt3x+, Polar Active accelerometer, Omron HJ-720 and Yamax Digiwalker SW-701 pedometer step counts in lab-based and free-living settings. *Journal of Sports Sciences*, *33*(10), 991–1000. https://doi.org/10.1080/02640414.2014.981848

Lee, J.-M., Kim, Y., & Welk, G. J. (2014). Validity of Consumer-Based Physical Activity Monitors. *Medicine & Science in Sports & Exercise*, *46*(9), 1840–1848. https://doi.org/10.1249/MSS.0000000000000287

Lee, P. H., Macfarlane, D. J., Lam, T., & Stewart, S. M. (2011a). Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *8*(1), 115. https://doi.org/10.1186/1479-5868-8-115

Léger, L., Lambert, J., Goulet, A., Rowan, C., & Dinelle, Y. (1984). [Aerobic capacity of 6 to 17-year-old Quebecois--20 meter shuttle run test with 1 minute stages]. *Canadian Journal of Applied Sport Sciences. Journal Canadien Des Sciences Appliquees Au Sport*, *9*(2), 64–69. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6733834

Leong, J. Y., & Wong, J. E. (2017). Accuracy of three Android-based pedometer applications in laboratory and free-living settings. *Journal of Sports Sciences*, *35*(1), 14–21. https://doi.org/10.1080/02640414.2016.1154592

Livingstone, M. B. E. (1997). Heart-rate monitoring: the answer for assessing energy expenditure and physical activity in population studies?. *British Journal of Nutrition*, *78*(6), 869-871.

Marin, T. S., Kourbelis, C., Foote, J., Newman, P., Brown, A., Daniel, M., … Clark, R. A. (2019). Examining adherence to activity monitoring devices to improve physical activity in adults with cardiovascular disease: A systematic review. *European Journal of Preventive Cardiology*, *26*(4), 382–397. https://doi.org/10.1177/2047487318805580

Mayorga-Vega, D., Aguilar-Soto, P., & Viciana, J. (2015). Criterion-Related Validity of the 20-M Shuttle Run Test for Estimating Cardiorespiratory Fitness: A Meta-Analysis. *Journal of Sports Science & Medicine*, *14*(3), 536–547. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/26336340

Mayorga-Vega, D., Bocanegra-Parrilla, R., Ornelas, M., & Viciana, J. (2016). Criterion-Related Validity of the Distance- and Time-Based Walk/Run Field Tests for Estimating Cardiorespiratory Fitness: A Systematic Review and Meta-Analysis. *PLOS ONE*, *11*(3), e0151671. https://doi.org/10.1371/journal.pone.0151671

McDade, T. W., Williams, S., & Snodgrass, J. J. (2007). What a drop can do: dried blood spots as a minimally invasive method for integrating biomarkers into population-based research. *Demography*, *44*(4), 899-925.

McDade, T. W. (2014). Development and validation of assay protocols for use with dried blood spot samples. *American Journal of Human Biology*, *26*(1), 1–9. https://doi.org/10.1002/ajhb.22463

McQueen, M. J., Hawken, S., Wang, X., Ounpuu, S., Sniderman, A., Probstfield, J., … INTERHEART study investigators. (2008). Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. *The Lancet*, *372*(9634), 224–233. https://doi.org/10.1016/S0140-6736(08)61076-4

Migueles, J. H., Cadenas-Sanchez, C., Ekelund, U., Delisle Nyström, C., Mora-Gonzalez, J., Löf, M., … Ortega, F. B. (2017). Accelerometer Data Collection and Processing Criteria to Assess Physical Activity and Other Outcomes: A Systematic Review and Practical Considerations. *Sports Medicine (Auckland, N.Z.)*, *47*(9), 1821–1845. https://doi.org/10.1007/s40279-017-0716-0

Miller, I. M., Lacher, D. A., Chen, T.-C., Zipf, G. W., Gindi, R. M., Galinsky, A. M., … Terry, A. L. (2015). Collection and laboratory methods for dried blood spots for hemoglobin A1c and total and high-density lipoprotein cholesterol in population-based surveys. *Clinica Chimica Acta*, *445*, 143–154. https://doi.org/10.1016/J.CCA.2015.03.028

Mora, S., Redberg, R. F., Cui, Y., Whiteman, M. K., Flaws, J. A., Sharrett, A. R., & Blumenthal, R. S. (2003). Ability of Exercise Testing to Predict Cardiovascular and All-Cause Death in Asymptomatic Women. *JAMA*, *290*(12), 1600–1607. https://doi.org/10.1001/jama.290.12.1600

Murakami, H., Kawakami, R., Nakae, S., Nakata, Y., Ishikawa-Takata, K., Tanaka, S., & Miyachi, M. (2016). Accuracy of Wearable Devices for Estimating Total Energy Expenditure. *JAMA Internal Medicine*, *176*(5), 702. https://doi.org/10.1001/jamainternmed.2016.0152

Myers, J., Kokkinos, P., Chan, K., Dandekar, E., Yilmaz, B., Nagare, A., … Soofi, M. (2017). Cardiorespiratory Fitness and Reclassification of Risk for Incidence of Heart Failure. *Circulation: Heart Failure*, *10*(6). https://doi.org/10.1161/CIRCHEARTFAILURE.116.003780

Myers, J., McAuley, P., Lavie, C. J., Despres, J.-P., Arena, R., & Kokkinos, P. (2015). Physical Activity and Cardiorespiratory Fitness as Major Markers of Cardiovascular Risk: Their Independent and Interwoven Importance to Health Status. *Progress in Cardiovascular Diseases*, *57*(4), 306–314. https://doi.org/10.1016/j.pcad.2014.09.011

Nguyen, Q. C., Whitsel, E. A., Tabor, J. W., Cuthbertson, C. C., Wener, M. H., Potter, A. J., … Harris, K. M. (2014). Blood spot–based measures of glucose homeostasis and diabetes prevalence in a nationally representative population of young US adults. *Annals of Epidemiology*, *24*(12), 903-909.e1. https://doi.org/10.1016/J.ANNEPIDEM.2014.09.010

Nolan, M., Mitchell, J. R., & Doyle-Baker, P. K. (2014). Validity of the Apple iPhone ® /iPod Touch ® as an Accelerometer-Based Physical Activity Monitor: A Proof-of-Concept Study. *Journal of Physical Activity and Health*, *11*(4), 759–769. https://doi.org/10.1123/jpah.2011-0336

O'Neill, B., McDonough, S. M., Wilson, J. J., Bradbury, I., Hayes, K., Kirk, A., … Tully, M. A. (2017). Comparing accelerometer, pedometer and a questionnaire for measuring physical activity in bronchiectasis: a validity and feasibility study. *Respiratory Research*, *18*(1), 16. https://doi.org/10.1186/s12931-016-0497-2

Phillips, L. R. S., Parfitt, G., & Rowlands, A. V. (2013). Calibration of the GENEA accelerometer for assessment of physical activity intensity in children. *Journal of Science and Medicine in Sport*, *16*(2), 124–128. https://doi.org/10.1016/j.jsams.2012.05.013

Pischon, T., Girman, C. J., Sacks, F. M., Rifai, N., Stampfer, M. J., & Rimm, E. B. (2005). Non–High-Density Lipoprotein Cholesterol and Apolipoprotein B in the Prediction of Coronary Heart Disease in Men. *Circulation*, *112*(22), 3375–3383. https://doi.org/10.1161/CIRCULATIONAHA.104.532499

Presset, B., Laurenczy, B., Malatesta, D., & Barral, J. (2018). Accuracy of a smartphone pedometer application according to different speeds and mobile phone locations in a laboratory context. *Journal of Exercise Science and Fitness*, *16*(2), 43. https://doi.org/10.1016/J.JESF.2018.05.001

Prince, S. A., Adamo, K. B., Hamel, M., Hardt, J., Connor Gorber, S., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *5*(1), 56. https://doi.org/10.1186/1479-5868-5-56

Rachim, V. P., & Chung, W.-Y. (2019). Multimodal Wrist Biosensor for Wearable Cuff-less Blood Pressure Monitoring System. *Scientific Reports*, *9*(1), 7947. https://doi.org/10.1038/s41598-019-44348-3

Rahbar, S. (2005). The Discovery of Glycated Hemoglobin: A Major Event in the Study of Nonenzymatic Chemistry in Biological Systems. *Annals of the New York Academy of Sciences*, *1043*(1), 9–19. https://doi.org/10.1196/annals.1333.002

Rothney, M. P., Schaefer, E. V., Neumann, M. M., Choi, L., & Chen, K. Y. (2008). Validity of Physical Activity Intensity Predictions by ActiGraph, Actical, and RT3 Accelerometers. *Obesity*, *16*(8), 1946–1952. https://doi.org/10.1038/oby.2008.279

Santos-Lozano, A., Santín-Medeiros, F., Cardon, G., Torres-Luque, G., Bailón, R., Bergmeir, C., … Garatachea, N. (2013). Actigraph GT3X: Validation and Determination of Physical Activity Intensity Cut Points. *International Journal of Sports Medicine*, *34*(11), 975–982. https://doi.org/10.1055/s-0033-1337945

Santos-Lozano, A., Hernández-Vicente, A., Pérez-Isaac, R., Santín-Medeiros, F., Cristi-Montero, C., Casajús, J. A., & Garatachea, N. (2017). Is the SenseWear Armband accurate enough to quantify and estimate energy expenditure in healthy adults? *Annals of Translational Medicine*, *5*(5), 97. https://doi.org/10.21037/atm.2017.02.31

Schoot, T. S., Weenk, M., van de Belt, T. H., Engelen, L. J. L. P. G., van Goor, H., & Bredie, S. J. H. (2016). A New Cuffless Device for Measuring Blood Pressure: A Real-Life Validation Study. *Journal of Medical Internet Research*, *18*(5), e85. https://doi.org/10.2196/jmir.5414

Schrack, J. A., Zipunnikov, V., Goldsmith, J., Bandeen-Roche, K., Crainiceanu, C. M., & Ferrucci, L. (2014). Estimating energy expenditure from heart rate in older adults: a case for calibration. *PLoS One*, *9*(4), e93520.

Schuch, F.B., Vancampfort, D., Firth., J., Rosenbaum., Ward, P.B., Silva, E., Hallgren, Dunn, AL., Deslandes, ., Fleck, MC., Carvalho, AF., & Stubbs, B., Schuch, F. B., Vancampfort, D., Firth, J., Rosenbaum, S., Ward, P. B., … Stubbs, B. (2018). Physical Activity and Incident Depression: A Meta-Analysis of Prospective Cohort Studies. *American Journal of Psychiatry*, *(in press)*(7), 631–648. https://doi.org/10.1176/appi.ajp.2018.17111194

Sharma, M., Barbosa, K., Ho, V., Griggs, D., Ghirmai, T., Krishnan, S., … Cao, H. (2017). Cuff-Less and Continuous Blood Pressure Monitoring: A Methodological Review. *Technologies*, *5*(2), 21. https://doi.org/10.3390/technologies5020021

Slinde, F., Bertz, F., Winkvist, A., Ellegård, L., Olausson, H., & Brekke, H. K. (2013). Energy expenditure by multisensor armband in overweight and obese lactating women validated by doubly labeled water. *Obesity*, *21*(11), 2231–2235. https://doi.org/10.1002/oby.20363

Strath, S. J., Kaminsky, L. A., Ainsworth, B. E., Ekelund, U., Freedson, P. S., Gary, R. A., … Swartz, A. M. (2013). Guide to the Assessment of Physical Activity: Clinical and Research Applications. *Circulation*, *128*(20), 2259–2279. https://doi.org/10.1161/01.cir.0000435708.67487.da

Swift, D. L., Lavie, C. J., Johannsen, N. M., Arena, R., Earnest, C. P., O'Keefe, J. H., … Church, T. S. (2013). Physical activity, cardiorespiratory fitness, and exercise training in primary and secondary coronary prevention. *Circulation Journal : Official Journal of the Japanese Circulation Society*, *77*(2), 281–292. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23328449

Tremblay, M. S., LeBlanc, A. G., Kho, M. E., Saunders, T. J., Larouche, R., Colley, R. C., … Gorber, S. (2011). Systematic review of sedentary behaviour and health indicators in school-aged children and youth. *International Journal of Behavioral Nutrition and Physical Activity*, *8*(1), 98. https://doi.org/10.1186/1479-5868-8-98

Troiano, R. P., McClain, J. J., Brychta, R. J., & Chen, K. Y. (2014). Evolution of accelerometer methods for physical activity research. *British Journal of Sports Medicine*, *48*(13), 1019–1023. https://doi.org/10.1136/bjsports-2014-093546

Trost, S. G., Mciver, K. L., & Pate, R. R. (2005). Conducting Accelerometer-Based Activity Assessments in Field-Based Research. *Medicine & Science in Sports & Exercise*, *37*(Supplement), S531–S543. https://doi.org/10.1249/01.mss.0000185657.86065.98

Tsimikas, S., & Hall, J. L. (2012). Lipoprotein(a) as a Potential Causal Genetic Risk Factor of Cardiovascular Disease. *Journal of the American College of Cardiology*, *60*(8), 716–721. https://doi.org/10.1016/j.jacc.2012.04.038

Tudor-Locke, C., Williams, J. E., Reis, J. P., & Pluto, D. (2002). Utility of Pedometers for Assessing Physical Activity. *Sports Medicine*, *32*(12), 795–808. https://doi.org/10.2165/00007256-200232120-00004

Tully, M. A., McBride, C., Heron, L., & Hunter, R. F. (2014). The validation of Fitbit Zip™ physical activity monitor as a measure of free-living physical activity. *BMC Research Notes*, *7*(1), 952. https://doi.org/10.1186/1756-0500-7-952

van Poppel, M. N. M., Chinapaw, M. J. M., Mokkink, L. B., van Mechelen, W., & Terwee, C. B. (2010). Physical Activity Questionnaires for Adults. *Sports Medicine*, *40*(7), 565–600. https://doi.org/10.2165/11531930-000000000-00000

Vasan, R. S., Larson, M. G., Leip, E. P., Evans, J. C., O'Donnell, C. J., Kannel, W. B., & Levy, D. (2001). Impact of High-Normal Blood Pressure on the Risk of Cardiovascular Disease. *New England Journal of Medicine*, *345*(18), 1291–1297. https://doi.org/10.1056/NEJMoa003417

Villars, C., Bergouignan, A., Dugas, J., Antoun, E., Schoeller, D. A., Roth, H., … Simon, C. (2012). Validity of combining heart rate and uniaxial acceleration to measure free-living physical activity energy expenditure in young men. *Journal of Applied Physiology*, *113*(11), 1763–1771. https://doi.org/10.1152/japplphysiol.01413.2011

WHO. (2017). Cardiovascular diseases (CVDs). Retrieved June 3, 2019, from https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

WHO | World Health Statistics 2018: Monitoring health for the SDGs. (2018). *WHO*. Retrieved from https://www.who.int/gho/publications/world_health_statistics/2018/en/

Wijndaele, K., Westgate, K., Stephens, S. K., Blair, S. N., Bull, F. C., Chastin, S. F. M., … Healy, G. N. (2015). Utilization and Harmonization of Adult Accelerometry Data. *Medicine & Science in Sports & Exercise*, *47*(10), 2129–2139. https://doi.org/10.1249/MSS.0000000000000661

Wilmot, E. G., Edwardson, C. L., Achana, F. A., Davies, M. J., Gorely, T., Gray, L. J., … Biddle, S. J. H. (2012). Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia*, *55*(11), 2895–2905. https://doi.org/10.1007/s00125-012-2677-z

Wilson, P. W. F., D'Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel, W. B. (1998). Prediction of Coronary Heart Disease Using Risk Factor Categories. *Circulation*, *97*(18), 1837–1847. https://doi.org/10.1161/01.CIR.97.18.1837

Wright, S. P., Hall Brown, T. S., Collier, S. R., & Sandberg, K. (2017). How consumer physical activity monitors could transform human physiology research. *American*

*Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *312*(3), R358–R367. https://doi.org/10.1152/ajpregu.00349.2016

Wu, W., Dasgupta, S., Ramirez, E. E., Peterson, C., & Norman, G. J. (2012). Classification accuracies of physical activities using smartphone motion sensors. *Journal of Medical Internet Research*, *14*(5), e130. https://doi.org/10.2196/jmir.2208

Yoon, Y.-Z., Kang, J. M., Kwon, Y., Park, S., Noh, S., Kim, Y., … Hwang, S. W. (2018). Cuff-Less Blood Pressure Estimation Using Pulse Waveform Analysis and Pulse Arrival Time. *IEEE Journal of Biomedical and Health Informatics*, *22*(4), 1068–1074. https://doi.org/10.1109/JBHI.2017.2714674

Zakeri, I., Adolph, A. L., Puyau, M. R., Vohra, F. A., & Butte, N. F. (2008). Application of cross-sectional time series modeling for the prediction of energy expenditure from heart rate and accelerometry. *Journal of Applied Physiology*, *104*(6), 1665–1673. https://doi.org/10.1152/japplphysiol.01163.2007